Reviewer's report

**Title:** Marginal Impact of Phenotypic Selection on Detecting MC4R Mutations in Italian Obese Children

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**Reviewer:** Giles Yeo

**Reviewer's report:**

In essence, the manuscript by Santoro et al provides us with the functional analysis on 2 new MC4R non-synonymous mutations, one of which, Q307X is a nonsense mutation and is consequently completely inactive. The functional analyses are well performed.

However, my main problem is with the conclusion that MC4R mutations are not identified by a 'particular phenotype'. I would have to disagree with this entirely, as patients with MC4R mutations have a very clear phenotype that has been well reported by Farooqi et al 2003, NEJM. Perhaps the authors meant to say that the prevalence of MC4R mutations in a highly selected Italian cohort of severely obese children is lower than in other areas of Europe? I would like to see the text of the abstract and conclusions changed to reflect this.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests